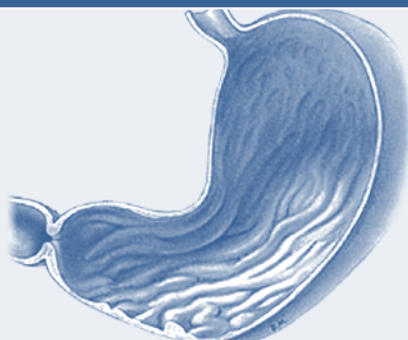


AMERICAN COLLEGE OF GASTROENTEROLOGY

UNDERSTANDING ULCERS, NSAIDs & GI BLEEDING



A CONSUMER HEALTH GUIDE



ACG. Digestive Disease Specialists
Committed to Quality in Patient Care.

The American College of Gastroenterology

The American College of Gastroenterology was founded in 1932 to advance the scientific study and medical treatment of disorders of the gastrointestinal tract. The College promotes the highest standards in medical education and is guided by its commitment to meeting the needs of clinical gastroenterology practitioners.

Table of Contents

Introduction	1
The Gastrointestinal Tract	2
GI Bleeding: What It Is and What It Is Not	2
Patients Can Have GI Bleeding Without any Obvious Symptoms	2
How Do You Recognize the Symptoms of GI Bleeding?	2
What are the Different Types of GI Bleeding?	3
Ulcers	4
What is an Ulcer?	4
What are the Symptoms of Ulcers?	4
What Causes Ulcers?	4
What Should I Know about <i>Helicobacter pylori</i> (<i>H. pylori</i>)?	5
What Should I Know about Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)	5
What are the Complications of Ulcers?	6
How are Ulcers Diagnosed?	6
Tests for <i>Helicobacter pylori</i>	6
How are Ulcers Treated?	6
NSAIDs: Issues that May Arise with Regular Use of NSAIDs	7
Background on COX-II Pain Medications	8
Practical Treatment Options for Chronic Pain from Arthritis and Other Causes	10
Magnitude of NSAIDs Use	11
Some Health Benefits Associated with Aspirin and NSAIDs	12
Balancing Pain Relief and Concerns with Side Effects	12
Acetaminophen – A Non-NSAID Pain Relief Option	13
Personal Medical History is Important to Understanding Your Risk	13
Important Considerations for Using NSAIDs	15
What Can You Do if You Are Concerned about Avoiding GI Bleeding?	15
Medications That May Be Taken to Inhibit or Reverse the NSAIDs-Induced Injury to the Intestinal Lining and GI Bleeding	16
Over-the-Counter NSAIDs	18
Prescription NSAIDs	19
Prescription COX-II Selective NSAIDs	19

Introduction

Gastrointestinal (GI) bleeding is an important, and potentially serious, condition. It can arise initially with few if any symptoms. Ulcers are injuries or damage to the intestinal lining that may result in GI bleeding. Ulcers can be promoted by the use of non-steroidal anti-inflammatory drugs, or NSAIDs. While some damage may occur with modest, short-term doses, problems are more likely to arise in regular NSAID users, and increase with the magnitude of use—more frequent use and/or higher dosages.

NSAIDs and aspirin have some very positive health benefits. Like all medications, care must be taken with their use. They should not be taken with alcohol, as the combination can increase the risk of GI bleeding. Patients who need to use NSAIDs regularly should consult with their physician on a regular basis to be alert for any potential GI effects. Problems may arise with few, if any, symptoms, but if they are recognized early, there are a variety of ways to minimize or reverse any adverse effects. Options include using alternatives to NSAIDs, or your physician prescribing medications that can reduce any adverse effects.

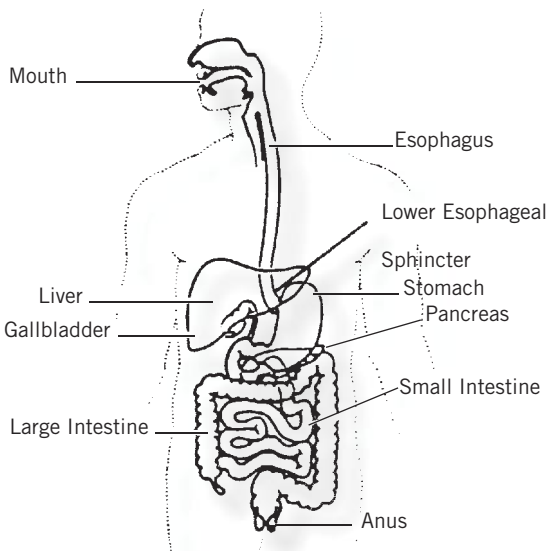


Figure 1: “The GI Tract”

The Gastrointestinal Tract

The gastrointestinal (GI) tract permits food to be made into nutrients that provide energy, and then allows the unused matter to be removed from the body. The GI tract starts with the mouth, where food is eaten, and follows to the esophagus, the stomach, the small intestine, the large intestine (colon) and the rectum. Other organs associated with the GI system include the liver, pancreas and gallbladder; these produce various substances that flow into the intestine to aid digestion.

GI Bleeding: What It Is and What It Is Not

When your physician speaks about GI bleeding, he/she is usually not talking about an external wound that results in visible bleeding from one or more GI organs, but rather means something more specific. Bleeding in the gastrointestinal tract means that some part of the body represented in the diagram on page 1 is bleeding internally, either slightly (which may or may not be very serious) or heavily (which may have serious health consequences).

2

Patients Can Have GI Bleeding Without any Obvious Symptoms

An individual can develop damage to the intestinal lining without being aware of it—significant GI bleeding occurs frequently without any symptoms being present.

How Do You Recognize the Symptoms of GI Bleeding?

Because GI bleeding is internal, it is possible for a person to have GI bleeding without having pain, literally without knowing you are bleeding. That is why it is important to recognize those symptoms that may accompany GI bleeding. The symptoms of possible GI bleeding vary, depending upon whether the source of the bleeding is in the upper part of the digestive tract (the esophagus, stomach or the beginning of the small intestine) or in the lower part (small intestine, colon or rectum).

Symptoms of Upper GI Bleeding:

- vomiting bright red blood
- vomiting dark clots, or material that looks like coffee grounds
- passing black, tar-like stool
- blood in the stool
- tiredness, shortness of breath due to iron deficiency anemia

Symptoms of Lower GI Bleeding:

- passing pure blood or blood mixed in stool
- bright red or maroon colored blood in the stool
- tiredness, shortness of breath due to iron deficiency anemia

What are the Different Types of GI Bleeding?

GI bleeding may come from various parts of the GI tract, and may be caused by various things:

Place	Type of Bleeding	Possible Reason(s)
Esophagus	Vomiting bright red blood or coffee grounds material Black stools	Ulcer, Varices*, Tear (forceful retching), Liver Disease, Chronic hepatitis
Stomach	Vomiting bright red blood or material that looks like coffee grounds Black stools	Ulcer, Swollen blood vessels in the stomach (known as varices)
Small Intestine	Bright red/maroon bleeding in stool	Ulcer, AVMs**
Large Intestine (Colon)	Blood in the stool	Colon Cancer, Polyps, Colitis, AVMs
Rectum	Bright red bleeding	Hemorrhoids, Tumor

* Varices = Esophageal varices are dilated blood vessels within the wall of the esophagus.

** AVMs = Arteriovenous malformations are abnormally dilated intraluminal blood vessels that often present as gastrointestinal bleeding.

Ulcers

About 20 million Americans will suffer from an ulcer in their lifetime. Duodenal (beginning of the small intestine) ulcers often occur between the ages of 30 and 50, and are twice as common among men. Stomach ulcers occur more often after the age of 60, and are more commonly seen in women.

What is an Ulcer?

Most GI bleeding comes from ulcers. An ulcer is an area of the lining of the stomach or duodenum that has been destroyed by digestive juices and stomach acid. The actual size of the ulcer can be very small (1-2 cm), but even small lesions can cause tremendous discomfort and pain.

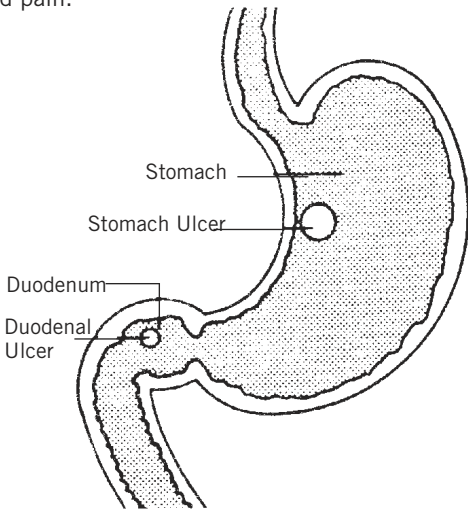


Figure 2: Stomach and Duodenum

What are the Symptoms of Ulcers?

The most common symptom of an ulcer is a gnawing or burning pain in the abdomen located between the navel and the bottom of the breastbone. The pain often occurs between meals and sometimes awakens people from sleep. Pain may last minutes to hours, and is often relieved by eating, taking antacids or acid blockers. Less common symptoms of an ulcer include nausea, vomiting and loss of appetite and weight, and bleeding.

What Causes Ulcers?

In the past, ulcers were incorrectly thought to be caused by stress. Doctors now know that there are two major causes of ulcers. Most duodenal and gastric ulcer

patients are infected with the bacterium *Helicobacter pylori* (*H. pylori*). Others who develop ulcers are regular users of pain medications called non-steroidal anti-inflammatory drugs (NSAIDs), which include common products like aspirin, ibuprofen, naproxen sodium and ketoprofen. The excessive or inappropriate use of over-the-counter NSAIDs can cause ulceration.

What Should I Know about *Helicobacter pylori* (*H. pylori*)?

The largest number of ulcers arise because of the presence of *H. pylori*. Because *H. pylori* exists in the stomachs of some people who do not develop ulcers, most scientists now believe that ulcers occur in persons who have a combination of a heredity/family predisposition, plus the presence of the bacterium, *H. pylori*.

The use of antibiotics to fight the *H. pylori* infection is a major scientific advance. Studies now show that antibiotics can permanently cure 80 to 90 percent of peptic ulcers. Blocking stomach acid remains very important in the initial healing of an ulcer.

What Should I Know about Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

The second major cause for ulcers is irritation of the stomach arising from regular use of non-steroidal anti-inflammatory drugs, or NSAIDs. NSAIDs are available over-the-counter (OTC) and by prescription.

If you are taking over-the-counter pain medications on a regular basis, you will want to talk with your physician about the potential for ulcers and other GI side effects. NSAID-induced gastrointestinal side effects can be reduced by using alternative therapy. Your doctor may recommend that you change the medication you are using; or add some other medication in conjunction with your pain medication.

Serious GI problems such as bleeding, ulceration and perforation often occur without warning symptoms in people using chronic NSAID therapy. Of particular concern are patients with arthritic conditions. More than 14 million such patients consume NSAIDs regularly. Up to 60 percent will have gastrointestinal side effects related to these drugs, and more than 10 percent will cease recommended medications because of troublesome gastrointestinal symptoms.

What are the Complications of Ulcers?

Bleeding: Internal bleeding in the stomach or the duodenum.

Perforation: When ulcers are left untreated, digestive juices and stomach acid can literally eat a hole in the intestinal lining, a serious medical problem that requires hospitalization, and often surgery.

Obstruction: Swelling and scarring from an ulcer may close the outlet of the stomach, preventing food to pass and causing vomiting and weight loss.

How are Ulcers Diagnosed?

The two tests most commonly used to evaluate for ulcers are an X-ray known as an Upper GI Series, or UGI, and a procedure called an Endoscopy, or EGD.

Endoscopy: This test involves insertion of a small, lighted flexible tube through the mouth into the esophagus, stomach, and small intestine (duodenum) to examine for abnormalities and remove small tissue samples (biopsy). The test is usually performed using medicines to temporarily sedate you.

Upper GI Series: Alternately, there is an X-ray test where you are given a chalky material (barium) to drink while X-rays are taken to outline the anatomy of the upper digestive tract.

6

Tests for *Helicobacter pylori*

There are several tests available to your doctor to evaluate for the presence of the bacterium, *H. pylori*. Samples of blood can be examined reliably for evidence of antibodies to the bacteria; a breath test can be examined for by-products from the bacteria; or biopsies from the stomach can be taken during upper endoscopy. New strategies include examining a sample of stool for the presence of bacteria, but this test is not widely available and has not been shown to be as reliable as breath tests or biopsies.

How are Ulcers Treated?

Diet: In contrast to past beliefs, diet has little to do with ulcer healing. Doctors now recommend that patients with ulcers only avoid foods that worsen their symptoms.

Smoking: Patients who smoke cigarettes should stop. Smoking has been shown to inhibit ulcer healing and is linked to ulcer recurrence.

Medical Therapy: Numerous medications which inhibit acid production can rapidly heal ulcers. Antibiotic therapy for *H. pylori* can accelerate healing and prevent recurrence. In general, ulcer patients should not take NSAIDs unless instructed to do so by their physician.

Surgical Therapy: When an ulcer fails to heal, or if complications of bleeding, perforation or obstruction develop, surgery may be necessary.

NSAIDs: Issues that May Arise with Regular Use of NSAIDs

Physicians and scientists have long recognized that every medication generally carries some risk associated with its use, and that using or prescribing a medication is prudent only when the benefits that can be derived from the medication outweigh its risks. Virtually everyone experiences pain and recognizes the huge potential benefit of pain relief or control. There are a significant portion of people who unfortunately are burdened with chronic, recurring pain from arthritis and other sources. For these people particularly, and to a lesser extent for those who experience pain less frequently, the task of balancing risks and benefits of pain relief has been a perennial problem for decades. Events and scientific findings over the past year have served to make this balancing act even more troublesome.

While all of us are familiar with the use of narcotic medications to control very serious pain following an operation or major traumatic injury, most of the time pain relief is attained by non-narcotic medications, some prescription medicines, and other products such as acetaminophen, aspirin, ibuprofen and naproxen that are available for over-the-counter purchase. These latter three drugs, as well as many non-narcotic prescription medications are from a class known as *non-steroidal anti-inflammatory drugs* or NSAIDs. It has long been recognized that persons using these NSAIDs are at a significantly increased risk of gastrointestinal complications, for instance, injury to the intestinal lining that can result in ulcers and/or gastrointestinal bleeding.

This is not a minor risk. With millions taking NSAID pain medications every day, it is estimated that more than 100,000 Americans are hospitalized each year and between 15,000 and 20,000 Americans die each year from ulcers and gastrointestinal bleeding linked to NSAID use.

Background on COX-II Pain Medications

Science has recognized that there are two types of enzymes which traditional medications of the type mentioned above reduce or inhibit. COX-II is the enzyme that triggers pain, and COX-I is the enzyme that protects the stomach from injury from acid or other irritants. Scientists learned years ago that they could fabricate a medication that stops the COX-II pain triggers without stopping the COX-I enzymes that protect the stomach.

The result was a new, apparently safer class of pain medication (at least for GI ulcers and bleeding risks) called COX-II inhibitors, prescription medications known as Celebrex[®], Bextra[®] and Vioxx[®]. The medications were used relatively safely by millions of chronic pain sufferers, captured a significant marketplace acceptance, and tended to provide a less risky alternative to traditional NSAIDs for chronic pain sufferers. By all appearances, this likely helped reduce the number of hospitalizations and deaths related to NSAID-induced ulcers and gastrointestinal bleeding.

Over the past year, much concern has been raised over COX-IIs, as scientific evidence came to light that patients taking some COX-II drugs were at greater risk of heart and cardiovascular problems than those not taking these drugs. In September, 2004, the manufacturer of Vioxx[®] (rofecoxib) announced that it was voluntarily withdrawing from the market in light of those findings. In February, 2005, the FDA Advisory Panel issued recommendations proposing new serious labeling warnings for Bextra[®] (valdecoxib) and Celebrex[®] (celecoxib) about increased cardiovascular risks, as well as expanded information about GI risks (ulceration and bleeding) for NSAIDs. Later in April, after it processed the Advisory Panel recommendation, FDA took the further step of asking the manufacturer to remove Bextra[®] from the market.

The FDA has indicated subsequently that it would consider (a) a proposal from the manufacturer to permit resumed marketing of Vioxx®; and (b) a proposal from the manufacturer for a program to provide limited access to Bextra® to those patients who think that it is the best medication for them. With respect to Celebrex®, as the sole COX-II pain relief agent still on the prescription market, FDA required four changes:

- (1) labeling change to incorporate data/findings on cardiovascular risk and detailed warnings about cardiovascular risk and risk of GI ulcer and bleeding;
- (2) encourage prescription at lowest possible dose for the shortest time;
- (3) provision of a Medication Guide to patients with their prescriptions to underscore cardiovascular and GI risks; and
- (4) commitment to study safety of Celebrex® vs. some traditional NSAIDs.

With all of these changes and warnings, it is not surprising that the number of prescriptions for COX-II inhibitors has declined significantly. This raises the related question of what pain medications are these patients taking if not a COX-II. Patients, and the physicians who treat them, are confronted with a fairly unpleasant choice that inevitably requires a detailed risk/benefit analysis among some less than perfect alternatives. Some chronic pain patients likely continue to take a COX-II inhibitor despite concerns about cardiovascular risks; some have reverted back to NSAIDs and are courting potentially increased risks of GI ulcers and bleeding. Others have likely switched to acetaminophen (Tylenol®) or other non-NSAIDs medication deemed to be more benign, and still others have reverted to traditional NSAIDs, but also take an additional medication to help reduce their risks to GI ulcers or bleeding. You should discuss with your physician the best treatment plan that is individualized for your particular healthcare risks.

Practical Treatment Options for Chronic Pain from Arthritis and Other Causes

- In recent years, many patients with chronic pain from arthritis and other causes have been treated with a class of apparently safer pain medications (at least for GI ulcers and bleeding) called COX-II inhibitors, such as Celebrex[®], Vioxx[®] and Bextra[®]. These drugs have offered relief and apparent reduced risks of GI bleeding, but recent reports raise significant concerns that these agents could be related to cardiac complications and potential liabilities which have adversely impacted acceptance, and may mitigate again use of COX-IIs in many patients.
- Practical treatment options/considerations may include:

Employing an alternative pain relief agent, e.g., use of acetaminophen (Tylenol[®]) which may be a satisfactory option:

- If this medication is sufficient to deliver pain relief,
- If the patient does not require anti-inflammatory aspects, *and*
- If patients do not regularly consume significant amounts of alcohol (potential dose related liver issues);

or

If patient needs require reverting to use of one of the traditional NSAIDs, adopting a combination therapy with either:

- (1) Misoprostol (Cytotec[®]) co-therapy which has been shown to reduce the risk of significant complications but whose use is limited by patient tolerance in approximately 30 percent of patients; *or*
- (2) Co-therapy with acid suppression medications such as a proton pump inhibitor. Two are currently approved by the FDA for NSAID users. Approved indications are healing and risk reduction of NSAID-associated gastric (stomach) ulcers (lansoprazole - Prevacid[®]) and risk reduction of gastric ulcers developing on continuous NSAID therapy (esomeprazole - Nexium[®]). Other proton pump inhibitors include the following medications: pantoprazole - Protonix[®], rabeprazole - Aciphex[®] and omeprazole - Prilosec[®] (the only one available over-the-counter).

There is another less powerful class of acid-suppressing agents (H₂ receptor agonists), available by prescription and over-the-counter including cimetidine - Tagamet[®]; famotidine - Pepcid[®]; nizatidine - Axid[®]; ranitidine - Zantac[®]. H₂ receptor agonists are less effective for acid suppression than proton pump inhibitors.

Magnitude of NSAIDs Use

Traditional NSAIDs (such as aspirin, ibuprofen and naproxen sodium) when taken routinely by patients for relief of chronic pain pose significant risk of gastrointestinal bleeding. At one time aspirin was virtually the only non-prescription pain reliever available. It has always had excellent pain relief benefits, but it was also recognized that, when used regularly, it could cause digestive problems for some patients. Some modified versions of aspirin came onto the market in an effort to achieve the benefits of aspirin while “buffering” the prospect for stomach discomfort, though subsequent experience evidenced that buffered aspirin did not reduce the risks of GI injury to any significant extent. Acetaminophen achieves similar benefits of pain relief, with reduced impact on the stomach lining.

New NSAID medications became available in prescription form that also offered excellent pain relief, but like aspirin, these new prescription medications also had the potential to promote the development of ulcers and bleeding in the GI tract. Since they were being administered under a doctor’s prescription, any such effects could be monitored.

NSAIDs became more popular as prescription remedies, and the FDA has approved several for sale to consumers without a prescription. FDA stated with respect to prescription strength NSAIDs including COX-II products such as Celebrex® (celecoxib) that these drugs need to include warnings of potential “increased risk of cardiovascular events and the well-described, serious potential life-threatening gastrointestinal (GI) bleeding associated with their use.” In conjunction with its actions related to prescription COX-II pain relievers, FDA required manufacturers of over-the-counter pain relievers to place warnings on their products about cardiovascular risks with, and GI risks of, these drugs and to remind patients to limit dose and duration of treatment. A partial list of NSAIDs that are available over-the-counter and recommended maximum daily doses can be found at the end of this brochure.

Currently, it is estimated that 20 million people in the U.S. have osteoarthritis and 2.1 million adults have rheumatoid arthritis, two conditions that often require regular/daily pain medication. NSAIDs are commonly prescribed for relief of pain and inflammation in these patients, so every day, more than 30 million people take NSAIDs. In fact, NSAIDs are the most prescribed class of medicines in the world. Unfortunately, each year, 16,000 die and 100,000 are hospitalized with GI complications.

Even some physicians may not recognize the risks of NSAID-associated ulcer and GI bleeding or that this can be a deadly condition without symptoms until bleeding occurs. When bleeding does occur, some patients will require intensive therapy with both endoscopic and pharmacologic intervention. As many as 60 percent of patients taking NSAIDs regularly over extensive periods of time may experience some side effect. So the risk is significant. You should feel free to talk to your doctor about these issues if he/she recommends NSAIDs, or take this brochure to the doctor's office.

Some Health Benefits Associated with Aspirin and NSAIDs

The main benefit recognized early on for aspirin was the relief of pain and the reduction in fever. Other important health benefits from aspirin have also come to be recognized. One of the more important of these is the use of aspirin in helping to prevent heart attack and perhaps stroke. The benefit stems from aspirin's role as a platelet inhibitor. Studies have shown that these benefits can be obtained with a relatively small daily dose of aspirin. While the current FDA labeling references a 325 mg dose for cardiac and cerebrovascular prevention, there is excellent evidence that these benefits could be attained with the lesser 81 mg dose, and a petition is pending with FDA seeking to modify aspirin labeling to shift to the 81 mg dose for this cardiac and cerebrovascular prevention. For these uses, more aspirin is not necessarily better, and you should consult your physician before beginning daily low dose aspirin.

NSAIDs were found to have an additional benefit of reducing inflammation, and so helped alleviate not only the symptom of pain, but also served to reduce the actual cause of the pain, e.g., reducing joint inflammation in arthritis.

Balancing Pain Relief and Concerns with Side Effects

Adverse side effects can accompany the benefits in a portion of patients taking any medication. No drugs escape the need for this kind of risk-benefit evaluation. It has become necessary to balance the benefits of analgesia, platelet inhibition, and anti-inflammatory effect from NSAIDs and aspirin against potential adverse effects on the stomach and digestive system. For patients who are dependent on regular use of pain relievers, this can mean determining whether there are alternate ways to achieve pain relief, without risking ulcers or

GI bleeding which may accompany regular use of aspirin and NSAIDs.

In this regard, aspirin and NSAIDs have been found to cause damage to the lining (or mucosa) of the digestive tract primarily in the stomach and upper intestine. This damage can result in an ulcer or intestinal bleeding. Although this can happen to an individual who is an infrequent user of aspirin or NSAIDs, it is of a much greater concern in frequent users, and those consuming higher dosages of these medications.

Acetaminophen – A Non-NSAID Pain Relief Option

Acetaminophen (Tylenol®) is a pain relief medication that is not an NSAID, and is not anti-inflammatory in its pain relief function. Acetaminophen therefore is not associated with either the cardiovascular or GI risks, and therefore is an important pain relief option that is generally considered more benign than NSAIDs. There has been some data reported to indicate that acetaminophen could have the potential to cause damage if it is used in high doses and/or combined with excessive alcohol consumption. Obviously, use of virtually any medication together with alcohol is ill-advised and risky. Patients taking acetaminophen doses that conform to the product's labeling and without alcohol, or even with moderate occasional social drinking, should not encounter any significant risks of these complications.

13

Personal Medical History is Important to Understanding Your Risk

As with any other risk-benefit analysis, the determination of the risk associated with a particular patient's use of NSAIDs requires a careful look at the patient's medical history. The key issues associated with NSAID-induced ulcers, GI injury and related bleeding include:

Previous Ulcer: A history of an ulcer, or an ulcer complication, have been identified in several studies as risk factors for complications due to aspirin or NSAIDs use.

Use of Multiple and/or High Dose NSAIDs: Adverse effects associated with NSAIDs become more likely as the cumulative amount of NSAID increases, relating both to the size of each dose you take, as well as frequency—how many times a day, how many days a week—you consume NSAIDs. Patients who take daily aspirin to reduce heart and/or stroke risk should recognize that low dose aspirin therapy represents a major risk factor for GI bleeding, particularly if you take daily doses of 325 mg.

Lower doses of 81 mg appear to have generally similar benefits with significant reduction in GI risks. Risks associated with daily aspirin are even more pronounced if patients also take other NSAIDs regularly.

Anti-coagulants: Similarly, patients who are taking NSAIDs at the same time they are taking oral prescription anti-coagulants (for example, medications like warfarin (Coumadin®)) have been found to have a twelve-fold increase in risk of bleeding.

Age: Has been identified as a risk factor in several studies. Older patients also often require pain medications more frequently, or in larger doses, further increasing their risk.

Steroids: Patients taking NSAIDs who also are taking a prescription corticosteroid, medications like prednisone (in doses over 10 mg), have been found to have a seven-fold increased risk of having GI bleeding.

Alcohol: Alcohol, taken alone can cause irritation of the GI tract. There have been some indications that patients who consume alcohol at the same time they are taking aspirin or NSAIDs have an increased risk of damage to the intestinal lining, including ulcers and GI bleeding. Chronic heavy alcohol users may be at increased risk of liver toxicity from excessive acetaminophen use. Individuals who consume large amounts of alcohol should not exceed recommended doses of acetaminophen. In 1993, FDA Advisory Committees recommended that all OTC pain relievers contain an alcohol warning: To date, some, but not all OTC pain relief products have complied with that recommendation. Chronic heavy alcohol users should consult their physician for advice on when and how to take pain relievers.

Important Considerations for Using NSAIDs

The most important ground rule, however, is to take a medication only as directed, and follow the instructions on your medication. No medication—whether a prescription or over-the-counter drug—should be taken more frequently than is directed in the labeling. Be familiar with potential side effects noted in the labeling and be on the lookout for them.

Some additional guidelines include:

- Tell your doctor about any medications you are taking, both prescription or over-the-counter.
- Avoid or limit alcohol usage while taking any NSAID.
- Stick to the minimum dose needed to treat the pain, for the minimum number of days and minimum number of times per day as absolutely necessary.
- Check ingredients and make sure to avoid taking several different medications containing NSAIDs at the same time.

Most NSAID ulcers heal easily if the NSAIDs are stopped. If the medication cannot be stopped, the dose may often be reduced. Even if your physician determines that continued administration of NSAIDs is needed, healing can still occur.

What Can You Do if You Are Concerned about Avoiding GI Bleeding?

If you are taking over-the-counter NSAIDs on a regular basis, you will want to talk with your physician about the potential for ulcers and other GI side effects. Most patients contact their family doctor, or primary care physician, when they experience GI problems. Many of these disorders, including *Helicobacter pylori*, can be treated readily by your primary care doctor.

In the case of recurring or more serious problems, you may need to see a gastroenterologist, a physician who specializes in disorders and conditions of the gastrointestinal tract. After completing the same training as all other physicians, gastroenterologists study for an additional two to three years to train specifically in conditions of the gastrointestinal tract.

Medications That May Be Taken to Inhibit or Reverse the NSAIDs-Induced Injury to the Intestinal Lining and GI Bleeding

ROLE FOR ACID SUPPRESSION/PROTON PUMP INHIBITORS TO REDUCE RISKS OF ULCERS AND GI BLEEDING

There are several factors stated elsewhere in this brochure, such as alcohol use and age, that increase risk of GI ulcer, injury or bleeding in those taking NSAIDs. Patients who have a history of prior ulcer disease or complications are believed to have the most significant risk factor for NSAID-induced GI complications, being two to four times more likely to have a GI ulcer, injury or bleeding if they take NSAIDs regularly.

In general, since most NSAIDs inhibit production of the enzyme that helps protect the stomach and intestinal lining from being damaged by stomach acid, reducing stomach acid is a good thing for those taking NSAIDs. Medicines that control or decrease acid in the stomach are considered a valuable palliative; if taken regularly while NSAIDs are used, they offer some protection to those who must take NSAIDs. Clinical studies suggest a 50 percent reduction in the formation of bleeding ulcers with the use of these medications.¹ The FDA recognizes specific benefits for NSAID users who are at high risk for gastric ulcers, and who take proton pump inhibitors, citing healing and risk reduction of NSAID-associated gastric (stomach) ulcers (lansoprazole - Prevacid®) and risk reduction of gastric ulcers developing on continuous NSAID therapy (esomeprazole - Nexium®). Other proton pump inhibitors include the following medications: pantoprazole - Protonix®, rabeprazole - Aciphex® and

¹ not all ulcers that may form in the stomach will eventually bleed.

omeprazole – Prilosec® (the only one available over-the-counter). There is another less powerful class of acid-suppressing agents (H_2 receptor agonists), largely over-the-counter products, including cimetidine – Tagamet®; famotidine – Pepcid®; nizatidine – Axid®; ranitidine – Zantac. H_2 receptor agonists are less effective for acid suppression than proton pump inhibitors.

Another medication, misoprostol - Cytotec®, has been used effectively to prevent gastric and duodenal ulcers and has been shown to reduce the risk of bleeding in those that must continue using NSAIDs. As with all instances where patients are taking more than one prescription or over-the-counter medication, patients and their physicians need to evaluate any side effects, potential drug interactions, or other factors, e.g. limitations on use during pregnancy.

Over-the-Counter NSAIDs

OTC Brand	Generic Name	Dose		
Actron®	ketoprofen	1-6 pills/day (up to 75 mg/day)		
Advil® Advil® Cold and Sinus Advil® Cold Advil®Allergy Sinus	ibuprofen	1-6 pills/day (up to 1,200 mg/day)		
Advil®, Children's Advil® Allergy Sinus	ibuprofen, pseudoephedrine hydrochloride, and chlorpheniramine maleate	weight (lbs)	age (yrs)	dose (tsp)
		48	6	Ask a doctor
		48-95	6-11	2-8 tsp/day (up to 800 mg/day ibuprofen, 120 mg/day pseudoephedrine hydrochloride, 4 mg/day chlorpheniramine maleate
Advil® Migraine Liqui-gels	ibuprofen	Adults: 2 pills/day (up to 200 mg/day) Under 18 years of age: ask a doctor		
Aleve®	naproxen sodium	1-3 pills/day* (up to 660 mg/day)		
Bayer®	aspirin	1-12 pills/day (up to 4,000 mg/day)		
Cap-Profen	ibuprofen			
Children's Elixure®	ibuprofen	weight (lbs)	age (yrs)	dose (tsp)
		< 24	< 2	ask a doctor
		24-35	2-3	1-4 tsp/day (up to 400 mg/day)
		36-47	4-5	1½-6 tsp/day (up to 600 mg/ day)
		48-59	6-8	2-8 tsp/day (up to 800 mg/day)
		60-71	9-10	2½-10 tsp/day (up to 1,000 mg/day)
		72-95	11	3-12 tsp/day (up to 1,200 mg/day)
Ecotrin®	aspirin	1-12 pills/day (up to 4,000 mg/day)		
Excedrin®	aspirin, acetamino- phen and caffeine	2-8 pills/day (up to 2,000 mg/day aspirin, 2,000 mg/day acetaminophen, and 520 mg/day caffeine)		
Ibuprohm® Ibuprohm® Cold and Sinus	ibuprofen			
Ibu-Tab 200®	ibuprofen			
Medipren®	ibuprofen			
Motrin IB®	ibuprofen	1-6 pills/day (up to 1,200 mg/day)		
Motrin, Children's Motrin® Cold	ibuprofen and pseudoephedrine hydrochloride	weight (lbs)	age (yrs)	dose (tsp)
		< 24	< 2	ask a doctor
		24-47	2-5	1-4 tsp/day (up to 400 mg/day ibuprofen and 60 mg/day pseudoephed- rine hydrochloride)
		48-95	6-11	2-8 tsp/day (up to 800 mg/day ibuprofen and 120 mg/day pseudoephedrine hydrochloride)
Nuprin®	ibuprofen	1-6 pills/day (up to 1,200 mg/day)		

*2-pill limit for patients over age 65.

OTC Brand	Generic Name	Dose
Orudis KT®	ketoprofen	1-6 pills/day (up to 75 mg/day)
Profen®	ibuprofen	
Sine-Aid IB®	ibuprofen and pseudoephedrine hydrochloride	
Tab-Profen®	ibuprofen	

Prescription NSAIDs

Prescription Brand	Generic Name	Dose
Actron®	ketoprofen	Talk to your doctor or pharmacist
Ansaid®	flurbiprofen	Talk to your doctor or pharmacist
Arthrotec® (combination with misoprostol)	diclofenac	Talk to your doctor or pharmacist
Cataflam®	diclofenac	Talk to your doctor or pharmacist
Combunox®	ibuprofen and oxycodone	Talk to your doctor or pharmacist
Clinoril®	sulindac	Talk to your doctor or pharmacist
Daypro®	oxaprozin	Talk to your doctor or pharmacist
Disalcid®	salsalate	Talk to your doctor or pharmacist
Dolobid®	diflunisal	Talk to your doctor or pharmacist
Feldene®	piroxicam	Talk to your doctor or pharmacist
Indocin® Indocin SR® Indo-Lemmon® Indomethegan®	indomethacin	Talk to your doctor or pharmacist
Lodine® Lodine XL®	etodolac	Talk to your doctor or pharmacist
Mobic®	meloxicam	Talk to your doctor or pharmacist
Nalfon® Nalfon 200®	fenoprofen	Talk to your doctor or pharmacist
Orudis®	ketoprofen	Talk to your doctor or pharmacist
Oruvail®	ketoprofen	Talk to your doctor or pharmacist
Ponstel®	mefenamic acid	Talk to your doctor or pharmacist
Relafen®	nabumetone	Talk to your doctor or pharmacist
Tolectin® Tolectin DS® Tolectin 600®	tolmetin	Talk to your doctor or pharmacist
Toradol®	ketorolac	Talk to your doctor or pharmacist
Vicoprofen®	ibuprofen and hydrocodone bitartrate	Talk to your doctor or pharmacist
Voltaren®	diclofenac	Talk to your doctor or pharmacist

Prescription COX-II Selective NSAIDs

Prescription Brand	Generic Name	Dose
Celebrex®	celecoxib	Talk to your doctor or pharmacist
Bextra®**	valdecoxib	Talk to your doctor or pharmacist
Vioxx®**	rofecoxib	Talk to your doctor or pharmacist

**Market availability of these products impacted by FDA decision process that began in February 2005 and is discussed earlier in this brochure.



American College of Gastroenterology

Digestive Disease Specialists
Committed to Quality in Patient Care

www.acg.gi.org

PRINTING MADE POSSIBLE BY AN EDUCATIONAL GRANT FROM TAP PHARMACEUTICAL PRODUCTS INC.

